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REMARKS

Claims 57-60 and 76-78 are pending in the subject application. No claim has been added, canceled or amended herein. Accordingly, claims 57-60 and 76-78 are still pending and under examination.

The Claimed Invention

This invention is based on the *surprising discovery* that inhibiting the interaction of RAGE and amphoterin inhibits tumor invasion in a local cellular environment.

Specifically, claims 57-60 and 76-78 provide a method for identifying an agent which inhibits tumor invasion in a local cellular environment. This method comprises: (a) providing a solid support coated with amphoterin; (b) contacting the solid support with a tumor cell which expresses receptor for advanced glycation endproducts (RAGE) under appropriate cell culture conditions for cell migration and growth; (c) admixing to the tumor cell culture of step (b) an agent to be tested; (d) determining the amount of spreading of the tumor cells on the solid support; and (e) comparing the amount of spreading of the tumor cells determined in step (d) with the amount of spreading determined in an identical tumor cell culture in the absence of the agent, wherein a decrease in the amount of spreading determined in step (d) indicates that the agent is identified as an agent which inhibits tumor invasion in the local cellular environment.

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Prior to the applicants' discovery, there was no reasonable expectation that inhibiting the interaction of RAGE and amphoterin would succeed in inhibiting tumor invasion in a local cellular environment.

Rejection under 35 U.S.C. §103(a)

In the Advisory Action, the Examiner maintained the rejection of claims 57-60 and 76-78 under 35 U.S.C. §103(a) as allegedly obvious over Hori et al. (J. Biol. Chem. 1995; 270(43):25752-25761) ("Hori") in view of Miki S et al. (Biochem. Biophys. Res. Commun. 1993 Oct. 29:196(2):984-9) ("Miki").

Applicants respectfully traverse the rejection of claims 57-60 and 76-78. In order to find the subject application obvious over Hori in view of Miki, the prior art references, in combination, must teach or suggest all the elements thereof, and create both a motive to combine and a reasonable expectation of success. Hori and Miki fail to do this.

Claims 57-60 and 76-78 are discussed above, as is the surprising discovery on which the claimed method is based.

It is again stressed that prior to the applicants' discovery, there was no reasonable expectation that inhibiting the interaction of RAGE and amphoterin would succeed in inhibiting tumor invasion in a local cellular environment. The Examiner's assertion of obviousness ignores this point.

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Specifically, the Examiner asserts that Hori teaches a method comprising the steps of coating a solid support with amphoterin, admixing sRAGE in the presence of neuronal cells expressing RAGE and measuring the binding of the cells to the solid support coated with amphoterin and also asserts that Miki teaches that renal cell carcinomas ("RCC") express RAGE. The Examiner then asserts that it would have been obvious for one of ordinary skill in the art to substitute tumor cells expressing RAGE for neuronal cells expressing RAGE into the method of Hori.

The Examiner has in no way shown how Hori in view of Miki teach or suggest applicants' invention which is based on the surprising finding discussed above. To maintain otherwise would constitute hindsight.

Furthermore, the Examiner has failed to show how Hori in view of Miki teach that if RAGE is expressed on a cell then inhibiting a single one of its ligand interactions would inhibit cell growth. The Examiner has also failed to show how Hori in view of Miki teach which particular RAGE/ligand interaction would have to be inhibited in order to inhibit cell growth. Finally, the Examiner has not shown art supporting the assertion that tumor cell behavior can be extrapolated from neuronal cell behavior.

Absent such a showing by the Examiner, the claimed method cannot be deemed to be *prima facie* obvious.

Accordingly, applicants maintain that the subject claims are not

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obvious over Hori in view Miki and therefore satisfy the requirements of 35 U.S.C. §103(a).

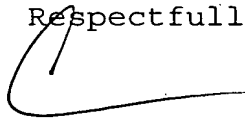
Summary

For the reasons set forth hereinabove, applicants respectfully request that all the claims of this application be allowed, and that the application proceed to issuance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
Tel. No. (212) 278-0400